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Simple and Compound Drugs in Late Renaissance Medicine: The Pharmacology of Andrea Cesalpino (1593)

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From antiquity, Galenic physicians extensively discussed the active powers of simple and compound drugs. In their views, simple drugs, that is, single ingredients, acted according to their material qualities and the properties of their substance. As for compound drugs, their efficacy resulted from the mutual interaction of their ingredients and their modes of preparation. In the late Renaissance, Galenic physicians and naturalists, such as Leonhart Fuchs and Pietro Andrea Mattioli, attempted to explain these pharmacological properties or "faculties" at the intersection of medicine, botany, and natural philosophy. This chapter examines the case of the Italian physician and botanist Andrea Cesalpino. His pharmacological treatise *De medicamentorum facultatibus* [*On the Faculties of Drugs*, 1593] was particularly significant for its reception of ancient and medieval medical texts on drug properties, *materia medica*, and the role of the senses in the knowledge of bodies.[1]

Appended to the second editions of his *Quaestiones peripateticae* [*Peripatetic Questions*] and *Daemonum investigatio* [*Investigation on Demons*] and the first edition of *Quaestiones medicae* [*Medical Questions*], Cesalpino's pharmacological treatise has passed unnoticed among historians of early modern science, whereas his *Quaestiones peripateticae* and *Investigatio* have raised more attention.[2] Indeed, his works were first devoted to Aristotelian natural philosophy and botany. It was in a later phase that he wrote on medicine, mostly therapy. In this regard, the *Quaestiones medicae* (1593) shows his interest in disease and treatment.[3] The first part of this treatise addresses a series of questions on the efficacy of drugs and poisons, as well as the types of fevers. The second part discusses various questions, such as phlebotomy, purgative drugs, sleep, and diet. In 1601, Cesalpino published a textbook on the art of healing, the *Κάτοπτρον, sive Speculum artis medicae Hippocraticum* [*Hippocratic Mirror of the Medical Art*].[4] This treatise systematically studies the general principles of therapy, fevers, poisons, syphilis, and skin diseases, before examining diseases in the traditional order from head to toe.

Among Cesalpino's medical works, *De medicamentorum facultatibus* is particularly important in bridging his medical training with his research on botany and mineralogy, as found in *De plantis* (1583) and the subsequent *De metallicis* (1596). In *De medicamentorum facultatibus,* instead of taking the viewpoint of a naturalist, Cesalpino discussed the powers and properties of substances as a learned physician trained in Galenic medicine.[5] It was from this angle that he offered his account of the medicinal powers of bodies, that is, "faculties" in relation to their nature, as well as their modes of preparation. Cesalpino's account referred as much to the tradition of *materia medica* and pharmacology as to Aristotelian natural philosophy. For Cesalpino, defining the active powers of drugs related to the components of bodies, their modes of transformation, and their relationship with the physician's sensory experience. By examining these questions, this chapter aims to provide an outline of Cesalpino's pharmacological theory at the crossroads of ancient, medieval, and Renaissance medical philosophy.

1. The Properties of Simple Drugs

The first part of Cesalpino's *De medicamentorum facultatibus* is centered on "simple" drugs, that is, single medicinal ingredients including food, minerals, and parts of plants and animals. To present their pharmacological properties, Cesalpino embraced the ethos of Renaissance humanism by referring to the ancient medical sources that were printed in Greek and translated into Latin in the Renaissance. The main reference in pharmacology was Galen's *On Simple Drugs*.[6] Following this treatise, early physicians framed the properties of drugs according to a determined scheme: the types of drug powers or "faculties" (*facultates*) according to their nature or temperament, their material structure, and their substance. While referring to the Galenic account of simple drugs and their faculties, Cesalpino also relied on the description and classification of drugs in ancient treatises of botany and pharmacy, overall, Theophrastus's *On the Causes of Plants* and Dioscorides' *Materia medica*.

Cesalpino followed the ancient pharmacological tradition by discussing several types of faculties of drugs.[7] The first faculties of drugs came from their temperament, that is, their constitution coming from the mixture of the four primary qualities—hot, cold, dry, and moist. These qualities resulted from the proportion of the four elements that composed bodies—air, fire, water, and earth. In addition, the second faculties of drugs came from the material texture of simple drugs, for instance, soft or hard, dense or loose, rough or smooth. The third and fourth faculties of drugs were associated with their substance. While the third had the capacity to attract, digest, or glue the body parts, the fourth acted on vital organs.

Such a typology of drug properties followed the principle of "curing by contraries," which was central to Galenic medicine. In humoral medicine, the patient was attributed a certain bodily temperament that came from the proportion of qualities. When the patient was sick due to a lack or an excess of these qualities, the physician prescribed a "contrary" remedy, which had an opposite temperament. For instance, an excessively

moist temperament was cured by a dry remedy, and a thick body part was healed by a thin remedy. Cesalpino adopted this Galenic framework to explain the properties of simple drugs, for instance, their cleansing, digestive, or cicatrizing powers coming from their temperament, that is, the proportion of their elemental qualities.

Cesalpino's conception of simple drugs highlighted the physician's task of determining the physical properties of bodies through the senses. To this purpose, he mostly summarized the fourth book of Galen's *On Simple Drugs* on the taste, odor, and color of drugs.[8] In his view, discussing the medicinal powers of plants, minerals, and animals required identifying their sensible properties, overall flavors, and, to a lesser extent, odors and colors. In particular, Cesalpino envisaged the list of seven flavors established by Galen and Aristotle.[9] The list comprised sweet, bitter, astringent, sour, acidic, salty, and acrid flavors. This classification was flexible as physicians tended to consider additional flavors. In this regard, Cesalpino expanded on the so–called "insipid" (*insipidus*), "fatty" (*pinguis*), and "nitrous" (*nitrosus*) flavors throughout his medical works.

It was mostly in considering the flavors of drugs that Cesalpino revealed his obedience to Aristotelian physics. Indeed, he aimed to show that the sensory properties of bodies came from the mixture of elements and qualities. Each flavor was characterized by a certain temperament, namely, a proportion of hot, cold, dry, and moist qualities, as well as a corresponding texture made of thick or thin parts. Such a framework, in turn, allowed the physician to infer the temperament and materiality of drugs through their very taste.

Remarkably, Cesalpino's gustative approach to drug powers also involved the properties related to the substance of bodies. In the Galenic tradition, drugs acting through their total substance included strong ingredients with poisonous or purgative effects. Whereas their effects were remarkable, they were difficult to explain through the action of the four qualities and were hence associated to their whole substance.[10] An influential interpretation that had emerged in the late medieval pharmacology, through works incorrectly attributed to the Persian physician Mesue (ibn Masawaiyh), was that such a substance had a celestial origin coming from their essence or "specific form."[11] Cesalpino, however, adopted a different standpoint. Whereas he related the strong properties of the total substance to the substantial form of drugs, he refuted any celestial nature for these powers. For Cesalpino, these powers came from the only material constitution and temperament of bodies, most notably, the complexity of their overall arrangement with respect to elements and qualities. This position meant that taste could be used too for assessing the properties of the total substance.[12] Such a stance about the role of the senses and the elemental nature of the total substance can be found across Cesalpino's medical works and it reflects, overall, his Aristotelian viewpoint on the nature and materiality of bodies. Following Aristotle, Cesalpino viewed drugs as tangible bodies made of elements, whose mixture defined their nature, that is, their primary and secondary qualities.

So far, we have seen that Cesalpino examined the role of the flavors to assay the constitution of simple drugs, that is their primary qualities and texture, and their related medicinal powers. Besides flavors, other sensory properties, such as odors and

colors, were discussed in his pharmacology according to Galen's account in *On Simple Drugs*. Although odors did not allow the physician to fully distinguish the properties of drugs in the same way that flavors did, Cesalpino examined them for their effects on the body.[13] Along the lines of Aristotle's *De sensu*, he broadly divided odors in pleasant and unpleasant types, with each having the same categories as flavors.[14] Most importantly, for Cesalpino, some odors had medicinal properties, as testified by the fragrance of flowers, ointments, and aromatic herbs. These types of odors were characterized by the proportion of the primary qualities, which could cure the constitution of the brain and the physiological spirits. Unpleasant odors could express medicinal powers, for instance, fumigations made of mineral bodies like sulfur and mercury, whose toxicity was beforehand mitigated by a careful preparation.[15]

As for colors, they hardly provided any clear indication of temperament because of their presence in each type of constitution.[16] Still, Cesalpino considered them according to the Aristotelian account of seven colors by including white (*albus*), yellow (*flavus*), purple (*puniceus*), red (*purpureus*), green (*viridis*), blue (*cyaneus*), grey (*fuscus*), and black (*niger*).[17] Each of them encompassed countless declinations and names. If these colors did not have specific medicinal properties, Cesalpino mentioned their role in theoretical and practical medicine.[18] In this regard, the color spectrum of urine was fundamental in uroscopy for diagnosing the patient, as shown by the Byzantine physician Actuarius (*c.* 1275–*c.* 1328) in *De urinis*.[19] In addition, Galenic physiology established different types of healthy and morbid humors with corresponding colors and flavors, mostly, variations of phlegm, bile, and melancholy. Furthermore, Cesalpino, as a Peripatetic physician, referred to the Aristotelian *De coloribus* to expand on the chromatic change of bodies in the physical world.[20] According to this treatise, colors were due to the reception of light on a surface rather than the mixture of primary qualities.

In emphasizing the various flavors, colors, and odors of many ingredients, Cesalpino pointed to the need for considering a series of natural factors, from climate, soil, and time to inner transformations such as combustion and coagulation. The vegetal realm, in particular, inspired two major arguments in his explanation. The ripening of fruits—from insipid, acidic, astringent, or sour to sweet—and wine production emphasized the role of taste in assessing the powers of simple drugs. On this point, Cesalpino drew on Galen's accent on the gradual transformation of grape into verjuice, ripe grape, and wine with its residual lees and flower, as well its transformation into alcohol and vinegar. These materials were the most obvious examples of how a same body might change in taste and texture, and how this process reflected the inner alteration in its very elements and qualities.[21]

In addition to the transformation of plants, mineral and metallic bodies raised the attention of Cesalpino, especially alkaline minerals, such as potash (*lixivium*) and saltpeter (*salnitrum*), which were used as detergent and fertilizer.[22] In examining their nitrous and acrid flavors, Cesalpino envisaged the formation of oils, acids, and combustible materials, either of natural origin, such as bitumen, or obtained through the art of distillation.[23] The ways of their formation mirrored Aristotle's account of terrestrial and aerial exhalations in the *Meteorology*.[24] This question also appealed for the mineralogical theory expounded in Cesalpino's 1596 *De metallicis*, where

he explained the formation and therapeutic use of numerous mineral and metallic ingredients in reference to Dioscorides' *Materia medica*. As we will see in this chapter, the strong powers of mineral and metallic drugs related to methods of drug preparation. Before examining this question, I shall now explore Cesalpino's account of compound drugs.

2. The Art of Drug Composition

Whereas a huge number of simple drugs could be used individually to cure simple diseases, Renaissance physicians and apothecaries combined simples in some cases. Usually, such compound drugs were used when the disease was complex in its symptoms or when the simple drug needed to be "corrected," that is, adjusted through a mixture with other simples. As Cesalpino underlined, the art of mixing ingredients into compound drugs was a longstanding practice among physicians, especially in Greek and Arabic pharmacy.[25] Galenic medicine celebrated theriac and mithridate as the most famous examples of how the pharmaceutical art of composition could produce powerful remedies and antidotes.[26]

Such a traditional line of thought underlay the second book of Cesalpino's *De medicamentorum facultatibus* on the properties of compound drugs.[27] The treatise was dedicated to the qualities and dosage of compounds, as well as their types of preparation. Throughout his exposition of compound drugs, Cesalpino mostly related to Galen's *On the Composition of Drugs According to Kind* and *Method of Healing*. In what follows, I examine Cesalpino's explanation of drug composition, including his general views on the mixture of their qualities and their transformation during diverse types of preparation.

Cesalpino first discussed the specificity and benefit of compound drugs in comparison with simple drugs. As he pointed out, "ostentation" (*pompa*) often motivated physicians and their rich patients to prefer sophisticated compounds based on a myriad of expensive ingredients, such as spices, gems, and precious metals. Yet, for Cesalpino, composing drugs was a useful pharmaceutical practice for therapy. According to Galen's *Method of Healing*, the art of drug composition was based on the general method of treatment, that is, on both reason and experience. Following this principle, physicians needed to determine the temperament of the patient to adjust his pharmacological treatment.[28] By combining different ingredients, they could adjust the qualitative balance of the resulting compound drug, for instance, by composing a hot and dry compound to cure a cold and moist disease.

The main simple drug, which was used as a basis (*radix*), might be mixed with additional ingredients to counterbalance its excessively strong, weak, noxious, or unpleasant nature.[29] Ingredients could also be harmonized by various types of preparation based on specific materials such as sugar and oil. One typical example came from Galen's recommendation for curing wounds.[30] While oil, wax, and verdigris as individual ingredients caused the infection of wounds, they produced an efficacious compound if mixed up into a plaster. Such a happy formula required the physician's knowledge of nature and temperament as a balanced mixture of qualities.

Compound drugs also offered the advantage of releasing the powers of their respective ingredients.[31] As Cesalpino explained, they were particularly efficacious to cure diseases with secondary infections following a certain order in their therapeutic effects. This reasoning was anchored in Galen's conception of *epikrasis*, namely the method of progressively replacing the noxious substance by a salutary one.[32] Following this method, Cesalpino expanded on the interaction of the ingredients according to their respective natures and relationships—"similar," "dissimilar," or "opposite"—in order to avoid their antagonism during their assimilation by the patient.[33] Such an approach offered the advantage of providing a progressive treatment of complex diseases with multiple causes and symptoms so to avoid the exhaustion of the patient.

For that purpose, physicians might mix similar ingredients, that is, simple drugs with the same temperament, in order to consolidate their powers or to heal several imbalanced conditions. The same reasoning went for the composition of dissimilar drugs to cure simultaneous diseases of different kinds. Opposite drugs followed the same path. As they did not act at the same time, they did not "cancel" each other. For instance, "attenuating" drugs operated before astringent drugs. It was in that very case that physicians could adjust the compound to the very constitution of the patient. Indeed, the temperament of the respective ingredients would balance and moderate each other, as Galen illustrated with the verdigris–based plaster. During this process, the respective qualities reached a medium so that the most intense qualities would be blunted.

The improvement or "correction" of drugs was another reason for combining simples. As Cesalpino noted, it was the treatise *De consolatione medicinarum* [*On the Consolation of Drugs*] attributed to Mesue that established the correction of drugs, yet only in the case of purgatives.[34] From this, Cesalpino set up six ways of correcting drugs. The first two ways consisted of correcting ingredients whose qualities were excessively strong or week. In this regard, the strengthening of drugs should follow the rule of affinity (*affinitas*), in reference to Pseudo-Mesue. For instance, agaric was corrected by ginger, aloe by cinnamon, and more broadly, by using sharp drugs with a hot and thin texture. The third way consisted of taming toxic ingredients, such as scammony. The fourth way aimed to improve the sensory features of drugs in order to make them more appealing, such as enhancing their taste by means of sugar, honey and wine, their color, and smell. The fifth way consisted of preparing the ingredient to facilitate its ingestion or application, for instance, through a mixture with a greasy substance in the case of ointments or with a beverage in the case of potions. The sixth way aimed to preserve drugs through a series of preparations within vinegar, salt, honey, and sugar, in the forms of preserves, electuaries, and syrups.[35]

While each of the ingredients of compounds acted with their own timing, they were also efficacious due to their mixing with other ingredients. In this regard, the powers of the total substance were typical of sophisticated compound drugs as they stemmed from the balance of all their ingredients. For instance, Cesalpino explained, theriac and antidotes were powerful because of their many ingredients, whose powers were slightly transformed by their mutual mixture. While their most toxic ingredients were tamed, the others retained some of their powers within the compound. This explained the efficacy of the compound to repel numerous ailments without injuring the patient.[36]

In order to combine simples in a way that would be efficient and safe, the constitution of each simple, in particular the intensity of its primary qualities, needed to be considered too. As Cesalpino pointed out, Galen and Dioscorides both emphasized that each quality could be either obscure, manifest, intense, or extreme to the senses. But it was the medieval Arabic-Latin texts provided by Al-Kindi, Averroes, and Arnald of Villanova that expounded on these levels of intensity, according to a gradual scale.[37] Following their views, Cesalpino comprised the level of intensity of each quality in a declination of four degrees, which the medical tradition called the "latitude" of temperament. His appraisal of the conception of degrees followed the idea that the qualities of bodies were relative to a scale between two extremes (hot and cold). Such a scale involved Galen's idea of a latitude of qualities through four degrees. Each degree corresponded to sensible variations that the human body could perceive, from almost imperceptible (first degree), to moderate (second degree), to harmful (third degree), to corrupted (fourth degree). Following this reasoning, Cesalpino established a latitude of eight parts between the extreme degrees of qualities, whose middle point (*medium*) was a temperate state.[38]

The knowledge of temperament and qualitative degrees was also important in the order of combination of simple drugs. Ingredients with the same qualities and similar degrees should be combined first.[39] Most importantly, the dosage of simple drugs within compounds should be smaller so to avoid toxic dosage of drugs with similar temperament and effects, especially in the case of psychoactive drugs and purgatives.[40] For instance, a purgative compound with cassia (whose dosage was twelve drachms) and rhubarb (whose dosage was two drachms) should combine six drachms of cassia with one drachm of rhubarb. The combination of simples with other ingredients was also an important aspect of their preparation, which Cesalpino expounded in a series of dedicated chapters.

3. The Types of Preparation

The last part of Cesalpino's book on compound drugs addressed a series of preparations that aimed to cleanse or transform the initial components. These included two main processes: filtration ("separation") and transformation ("alteration").[41]

The preparation of drugs by separation aimed to separate their "earthy," that is, their consistent part through washing or extraction. Washing (*ablutio*) removed the useless parts of an ingredient, for instance, ash from a burnt substance, fat from a greasy substance, or sand from minerals, in order to keep its main part and retain its powers. The typical ingredients subject to washing were hot and dry, with an acrid, bitter, or salty flavor. The resulting drug was more temperate, with a thicker and colder nature, since its thinner and hotter part remained in the washing liquid. Another type of separation included the extraction (*extractio*) of juices and oils from fruits, herbs, bulbs, and gums. Pressed oil was typically used for healing wounds through plasters and poultices, and to cure dry throat through "eclegmas."

Alteration aimed to transform the powers of drugs by fire through two main processes: decoction (*decoctio*) and distillation (*distillatio*).[42] As Cesalpino explained,

decoction in water, called *elixatio* (boiling), liquefied substances by loosening their parts. In the process, some powers disappeared, such as purgative properties and smell, while other remained, such as astringent properties.[43] The transformation of drugs by decoction also depended on the duration and the intensity of the fire. Mild decoctions included using a bain-marie (*in balneo*) and steam (*vapor*).

Preparation by alteration could also consist of cooking simple drugs with additional ingredients into liquid (rob, syrup, julep) or solid drugs (lozenges, pills).[44] For instance, syrups were made of an ingredient cooked with sugar or honey, robs through the cooking of fruit juice. These sweet ingredients offered the advantage to thicken these drugs and soften their powers, as well as to improve their taste and prolong their preservation time. Otherwise, simple drugs could be cooked with non-sweet substances. In this regard, purgatives like hellebore required slow cooking in combination with mastic in order to preserve their medicinal powers.[45]

Distillation both transformed and separated drugs. Cesalpino called "distillation" (*distillatio*) the separation of liquor, and "sublimation" (*sublimation*) the separation of a dry exhalation from a substance.[46] It was through these specific processes that Cesalpino expressed his position toward alchemy. In his view, alchemists (*chimisti*) considered distillation a technical art capable of purifying the elements of bodies in order to prevent them from putrefying, a phenomenon that had been confirmed by the conservation of distilled waters. Such a process, Cesalpino went on, aimed to obtain liquors, powders, and "ashes," as well as to introduce a golden or silver tincture into metals for their transmutation. As Cesalpino deplored, alchemists attempted to apply this process to medicine through the making of elixir and quintessence. Whereas he considered these materials as vain panaceas, he still proposed to examine what was useful for pharmacy in the alchemical art.[47]

Along the lines of the physicians and naturalists of his time, Cesalpino was attentive to the nature of the different phases of distillation. First, he noted, a thin part, made of air and water, evaporated, then thicker parts made of earth were separated under a longer and more intense fire. In the case of wine, the distilled liquor was a thin and airy, highly combustible, substance, namely *aqua ardens* (brandy). The residues of the distilled material provided a liquor made of earth and fire, whose caustic powers were comparable to lime. From this account, we see that Cesalpino considered the phases of distillation according to the Aristotelian physics of elements and qualities, rather than the alchemical notions of mercury, sulfur, and salt that were proposed by followers of Paracelsus.[48]

For Cesalpino, the first liquor extracted by distillation had medicinal properties because of its spirituous and fragrant substance. Made of very thin parts, it could easily penetrate the body and revive its physiological spirits, which had the same subtle constitution.[49] Distilled rose water was an example of aqueous humor with some aerial fragrant part. Cesalpino explained the formation of distilled waters through the case of cinnamon: its fragrant and fiery part was extracted in the form of an ascending vapor in the upper part of the cucurbit, which condensed into water by cooling down in the alembic.

The oil coming from the second phase of distillation was more difficult to execute. It came from the separation of an aerial and viscous part that surfaced from water,

in the example of the distilled oil of lavender seeds and anise. As Cesalpino noted, distilled oils were thinner and hotter than pressed oils. He also specified that pressed oils could be distilled but needed to be mingled with pieces of marble, glass, or sand in the cucurbit, to regulate the process of boiling. Following Pseudo-Mesue, he added the example of distilled oil of tiles (a similar material to oil of bricks), whose acrid substance was comparable to naphtha. Bitumen as well as resinous materials such as amber, pitch, and myrrh were also involved in the distillation of oils.[50]

Overall, Cesalpino's discussion on distillation reflected the common knowledge of plant distillation (flowers, woods, and seeds) for pharmaceutical purposes.[51] What was at stake was the possible preservation of sensory properties in distilled waters and oils. For instance, roses, lavender seeds, and cinnamon provided fragrant distillates that could heal the bodily spirits. In addition, distilled oils such as balsam were prescribed for their fatty and hot properties calming neuro–inflammation. The distilled waters of plants retained the powers of their initial ingredients only if they preserved their aerial part, which was responsible for their fragrant or acrid properties, or their aqueous part. The aerial substance could easily disappear during distillation, and hence it was required to heat up materials in a bain-marie. Cesalpino found distilled waters better to cure putrid fevers than decoctions and juices, because of their incorruptible nature. Distilling waters also offered the advantage of removing the astringent properties of plants, which remained in the thick part of the plant. At any rate, the distillation apparatus should be devoid of lead vessels, which would imbue distilled waters with a toxic led-based substance in the example of ceruse. Moreover, "circulatory" vessels (pelicans) could also be used to extract thicker waters within a single crucible through the circulation of steam.[52]

Outside of plants, minerals, such as alum, chalcanthite, and antimony, also provided medicinal waters and oils extracted by distillation. Indeed, mineral and metallic materials produced an acrid water as well as a thick liquor under a strong fire. Such distillates required special apparatus: namely, small glass cucurbits buried in mud to support a long fire, whose fumes descended into larger vessels. From a therapeutic angle, metallic distillates provided caustic oils that were useful to halt gangrene.[53] Nonetheless, Cesalpino insisted that most of the time plant decoctions and juices were enough to cure diseases.[54]

Not only did minerals provide distilled waters and oils, they also supplied powders and salts through the alchemical process of sublimation.[55] As Cesalpino explained, sublimation consisted of extracting dry exhalations in the form of some "ashes," namely transforming solid materials into fumes. This process was immediately followed by their condensation into a whitish powder as they cooled down on the lid of the crucible. According to Cesalpino, sublimation had been known since Dioscorides, who mentioned the processing of pitch and resin ashes, as well as burnt pyrites.[56] Indeed, sublimation allowed to obtain the dry and earthy part of materials. Their exhalation (fumes) cooled down into some earthy substance with hot and bitter properties, which had been observed since Galen. In the case of silver and bronze, the earthy substance ascended in the form of yellowish or white slags (*cadmia*) on the upper side of the oven. These slags, in turn, were the basis for making pompholyx and spodium, whose washing would leave out their caustic properties and allowed physicians to use them safely as desiccants.[57]

Sublimation could also be used for softening the toxic powers of sulfur, orpiment, and quicksilver.[58] For instance, quicksilver could be sublimed with sal ammoniac into a "sugar" (*saccharum*) called "sublimate" (*sublimatum*), that is, mercury bichloride. In late Renaissance medicine, such "corrosive sublimate" was used as a "caustic" topical remedy to cure wounds. For Cesalpino, these properties were due to its very hot and thin properties. Orpiment could also be sublimed as realgar into some white arsenic, with a translucent and crystalline texture. As for sulfur, it could be sublimed with quicksilver into cinnabar (mercury sulfide), a corrosive substance. In sum, for Cesalpino, sublimation offered the advantage of separating the exhalations of materials by increasing the degree of their heat, hence producing caustic drugs.[59] Following Galen, he broadly agreed on the preparation by fire (per ignem) as a way to improve certain ingredients by giving them new properties and by taming their strength and taste with a view of further medicinal preparations.[60]

4. Conclusion

Cesalpino's discussion of drug properties provides a striking example of how late Renaissance medical humanism was applied to pharmacology. At first, his discussion on the "faculties" of drugs confirms the appeal for the ancient Greek sources of pharmacology, overall, Galen. Nonetheless, Cesalpino's exposition of compound drugs also reveals his deep interest in medieval medicine. He was aware of the critical reception of the scholastic framework of pharmacological degrees in his own time. Nonetheless, Cesalpino believed the discussion necessary given the difficulty of predicting the qualities of compound drugs. In this way, he proved that the authority of Arabic–Latin texts was still strong in late sixteenth-century pharmacology.

In addition, Cesalpino discussed the art of separating body parts by the fire, that is, alchemy. Whereas he considered as vain the promises of immortality brought by medicinal elixir and quintessence, he acknowledged the usefulness of distillation and sublimation for drug making. For Cesalpino, distillation pointed to the relationship between the three phases of bodies and the "faculties" that he put forward in the first part of his treatise on simple drugs: elemental qualities, texture, and sensory properties. Following the Aristotelian physics of elements and qualities, the aqueous phase of distillation consisted of an aerial and thin body, the solid phase corresponded to a terrestrial and thick body, and the oily phase was a hot and thin body.

Within this Galenic and Aristotelian frameworks, Cesalpino put forward the role of the senses to appraise the active powers of drugs. Indeed, it was according to the sensorial world of physicians and botanists, namely in relation to taste, odor, and color, that he framed the types of physical and medicinal qualities. However, whereas it would be tempting to recollect a definite set of qualities for each medicinal ingredient, Cesalpino's treatise suggested the opposite reasoning for its in-depth discussion of their possible variations depending on their provenance or type of transformation. Beyond the extended classifications that existed in both pharmacological and botanical literature, Cesalpino blurred the boundaries between medicinal, physical, and sensible properties by taking the example of a select number of substances from vegetal,

mineral, and (more rarely) animal realms. Similarly, his discussion of the theoretical models for the composition of simple drugs emphasized the tension between the qualitative approach to bodies in view of their infinite variety within nature.

Notes

1 Andrea Cesalpino, *De medicamentorum facultatibus libri duo* (Venice: Giunta, 1593), fols. 242r–291v. I will refer to this treatise as *DMF* in the subsequent notes.

2 See for instance Andrea Strazzoni, "Cesalpino, Andrea," in *Encyclopedia of Renaissance Philosophy*, ed. Marco Sgarbi (Cham: Springer, 2022), 1:689–91; Carlo Colombero, "Andrea Cesalpino e la polemica anti-Aristotelica e anti-Spinoziana," *Rivista Critica di Storia della Filosofia* 35 (1980): 343–56; Mark E. Clark and Kirk Summers, "Hippocratic Medicine and Aristotelian Science in the *Daemonum investigatio peripatetica* of Andrea Cesalpino," *Bulletin of the History of Medicine* 69, no. 4 (1995): 527–41.

3 Andrea Cesalpino, *Quaestionum medicarum libri duo* (Venice: Giunta, 1593), fols. 170r–241v.

4 This treatise was also published as *Praxis universae artis medicae* [*Practice of the Whole Medical Art*], a systematic study on disease and treatment, which was reprinted in 1602–6, 1666, and 1670. On this text, see R. Allen Shotwell's contribution to this volume.

5 On Cesalpino's pharmacological theory, see Frederick W. Gibbs, *Poison, Medicine, and Disease in Late Medieval and Early Modern Europe* (New York: Routledge, 2019), 208–9. On his botanical works, see Brian W. Ogilvie, *The Science of Describing: Natural History in Renaissance Europe* (Chicago: Chicago University Press, 2006), 223–6. See also Fabrizio Baldassarri's, and Quentin Hiernaux's and Corentin Tresnie's contributions to this volume.

6 Galen, *De simplicium medicamentorum temperamentis et facultatibus*, 11:379–892K, 12:1–377K.

7 Cesalpino, *DMF*, fol. 242r: "Cum autem facultates vel in primis qualitatibus consistant, ut calefaciendi, refrigerandi, humectandi, et siccandi; vel in secundis, ut emolliendi, indurandi, rarefaciendi, condensandi, et aliis huiusmodi; vel in tertiis, ut glutinandi, concoquendi, abstergendi, repellendi, et tandem quae opera magis particularia et partes peculiares respiciunt, quae inter quartas facultates recenseri possunt, ut gignendi lac, et semen, ex obstruendi, hepar, lienem: aut roborandi cor, cerebrum, ventriculum, unde hepatica medicamenta, cephalica, stomachica, cordialia, et alia huiusmodi dicuntur."

8 Galen, *De simplicium medicamentorum temperamentis et facultatibus* 4.1–23 (11:619–703K).

9 See Galen, *De simplicium medicamentorum temperamentis et facultatibus* 4.1–4.13 (11:619–62K); Aristotle, *Sens.* 4.442a15–20.

10 See Linda Deer Richardson, "'The Generation of Disease: Occult Causes and Diseases of the 'Total Substance'," in *The Medical Renaissance of the Sixteenth Century*, ed. Andrew Wear, Roger K. French, and Iain M. Lonie (Cambridge: Cambridge University Press, 1985), 175–94; Gibbs, *Poison, Medicine, and Disease*, 195–204.

11 Pseudo-Mesue, *De consolatione et electione simplicium medicinarum, seu Canones universales*, 1.1, in *Opera omnia* (Venice: Valgrisi, 1562), fol. 2r. Paula De Vos, *Compound Remedies: Galenic Pharmacy from the Ancient Mediterranean to New*

Spain (Pittsburgh: University of Pittsburgh Press, 2021), 71–8. On Pseudo-Mesue, see also Dag Nikolaus Hasse, *Success and Suppression: Arabic Sciences and Philosophy in the Renaissance* (Cambridge : London, 2016), 10, 391–6.

12 Cesalpino, *DMF*, fol. 243r: "Soli autem sapores certius et propinquius non solum temperamentum ostendunt in calido frigido humido et sicco sed et reliquas facultates longe efficaciores tum ad morbos gignendos, tum sanandos."

13 Ibid., fols. 255v–260r.

14 Aristotle, *Sens.* 5.443b19–444a8.

15 Cesalpino, *DMF*, fol. 260r: "Alii ad morbum gallicum suffumigia parant sudatoria ex cinnabrio factitio, quod ex argento vivo et sulphure fit, quamvis genere sit deleterium. Praeparatio enim vitia corrigit."

16 Ibid., fols. 260v–261r: "Ex coloribus incertam esse temperamenti significationem … quod in unoquoque colore et calida et frigida et humida et sicca reperiuntur."

17 Ibid., fols. 261r–266r.

18 Ibid., fol. 261r: "Scientiam de coloribus in medicina ad multa alia utilem habebimus. Quod tanto libentius efficiam, quanto ab aliis hanc partem alioqui difficillimam, minus elaboratam perspicio."

19 See for instance Cesalpino, *DMF*, fol. 261r: "Albi igitur differentiae sex notantur ab Actuario in urinis: chrystalleus, niveus, aqueus, lacteus, glaucus, et charopus."

20 Ibid., fols. 263v–264v.

21 Ibid., fols. 249r–250r.

22 Ibid., fols. 252v–254v.

23 Ibid., fol. 253r: "Nitrosum iure in medio est; nam non omnino eius salsugo ab exhalatione combustibili absolvitur, ut patet in terrae salsugine, ex qua salnitrum extrahitur, ardet enim. Reliqua tamen genera nitri ad naturam salis magis accedunt, nam et inodora sunt et sine pinguedine, at carent astrictione."

24 See Aristotle, *Mete.* 1.4.341b6–18.

25 Cesalpino, *DMF*, fols. 267v–268r: "Quod si compositiones a clarissimis medicis non sine ratione excogitatas esse credendum est. Celebrantur enim a Galeno innumerae et a se inventae et ab antiquioribus. Arabes quoque multas in usum invexerunt, quibus frequenter hodie utimur felicissimo successu."

26 On theriac and mithridate in early modern medicine, see Alisha Rankin, *The Poison Trials: Wonder Drugs, Experiment, and the Battle for Authority in Renaissance Science* (Chicago: University of Chicago Press, 2021), 23–50.

27 See Cesalpino, *DMF*, fols. 266v–291v.

28 Galen, *Methodus medendi* 2.3 (10:85–93K).

29 Cesalpino, *DMF*, fols. 269v–271r.

30 Galen, *De compositione medicatorum per genera* 1.1 (13:362–67K); Galen, *Methodus medendi* 3.2 (10:162–73K).

31 Cesalpino, *DMF*, fols. 268r–269v.

32 Galen, *Methodus medendi* 9.10 (10:635–40K).

33 Cesalpino, *DMF*, fol. 268v: "Si igitur similes fuerint affectus, similia videntur exposcere remedia, si dissimiles dissimilia, si contrarii etiam contraria, seu plures morbi, seu plures causae, seu symptomata affuerint, quae sigillatim remedia exposcant, unde compositio tum similium, tum dissimilium, aut contrariorum necessaria esse videtur."

34 Pseudo-Mesue, *De consolatione*, fols. 1v–44r; De Vos, *Compound Remedies*, 91–8; Cesalpino, *DMF*, fol. 269v: "De hac re diligentissime egit Mesues … at solum de medicamentis purgantibus locutus est."

35 Ibid., fols. 269v–271r.
36 Ibid., fol. 269v: "Fieri tamen posse credendum est, ut etiam mixtum ratione componentium agat eas operationes, quae non ratione primarum qualitatum, sed secundarum et sequentium, et quae a tota substantia dicuntur, fiunt. Cum enim in mixtione non corrumpantur miscibilia, sed alterentur tantum, multas facultates eorum servari credendum est, quae permanent integra, cum praesertim ars non perfecte misceat. Sic theriacae compositio extat remedium ad omnia venena, quia in ea acervata sunt omnia, quae ad singula faciunt. Huiusmodi sunt et alia antidota a Graecis Polychresta appellata, quia ad diversos usu accommodantur propter multorum simplicium receptionem."
37 Michael McVaugh, "The Development of Medieval Pharmaceutical Theory," in *Arnaldi de Villanova Opera medica omnia II: Aphorismi de gradibus*, ed. Michael R. McVaugh (Barcelona: Universidad de Barcelona, 1981), 1–136.
38 Cesalpino, *DMF*, fol. 272r: "In intermedia autem latitudine variam ubique proportionem esse caliditatis et frigiditatis, unde gradus praedicti oriuntur …. Appellant autem medici principium medium et finem cuiusque gradus."
39 Ibid., fols. 281v–282r.
40 Ibid., fols. 282r–283v.
41 Ibid., fols. 283r–284r.
42 Ibid., fol. 284v: "Alii porro sunt modi separationis per decoctionem, et distillationem, seu sublimationem, qui non sine manifesta alteratione per ignem perficiuntur."
43 Ibid., fols. 284v–285v.
44 Ibid., fols. 285v–286r.
45 Ibid., fol. 286r: "Quidam eo artificio ex radicibus ellebori nigri succum extrahunt, qui ciceris magnitudine haustus addito mastiche purgat sine noxa."
46 Ibid., fols. 286r–287v.
47 Ibid., fol. 286v: "Laticem suum celebrantes immunem ab omni putredine, qui elixir ab ipsis vocatur, et quinta essentia, ad omnes morbos etiam incurabiles, ut promittunt, sanandos. Sed videamus quid in distillatione et sublimatione medicamenta patiantur; hinc enim patere possit, quae utilitas ex hac arte in medicina praestetur."
48 On the development of alchemy in early modern Italy, see Antonio Clericuzio, "Chemical Medicine and Paracelsianism in Italy, 1550–1650," in *The Practice of Reform in Health, Medicine, and Science, 1500–2000*, ed. Margaret Pelling and Scott Mandelbrote (London: Routledge, 2005), 59–79.
49 Cesalpino, *DMF*, fol. 286v: "Solus igitur primus liquor retinet vini aliquas facultates, spirituosam scilicet substantiam odoratam a reliquo corpore separatam, quae multas utilitates affere potest. Nam citissime omnium pervadit ad intima corporis, substantia affinis naturae humanae spiritus reficiens et calefaciens, non tamen relinquens impressionem caliditatis ob maximam tenuitatem."
50 Ibid., fol. 287r: "Mesues docet ex oleo communi, quod ab ignitis laterculis, cum in eo extinguuntur, absorbetur, deinde confractis iisdem et in distillatorio conditis, acerrimam substantiam elicere aequipollentem naphtae. Sunt qui ex lapidibus bituminosis et ex electro sine ulla admixtione simile oleum eliciant."
51 Ibid., fols. 287v–288v.
52 Ibid., fol. 288r: "Species quaedam distillationis est, cum aqua non in aliud vas recipiens colligitur, sed iterum descendit, unde egressa est, ac veluti per circulum saepius ascendit ac descendit, in qua operatione solvuntur magis partes corporis in liquorem crassiorem veluti succum."

53 Ibid., fol. 288r: "Ex chalcantho privatim id genus olei quaeritur, causticum ad gangraenas sistendas; audent quidam etiam intus exhibere guttam unam aut duas cum iusculo ad putredines internas malignas in peste."
54 Ibid., fol. 288r: "Ex quibus colligere licet, si quis egeat omnibus facultatibus, quae in medicamento sunt, nequaquam ei opus esse distillatis uti, sed longe melior erit succus aut decoctio."
55 Ibid., fols. 288v–289r.
56 Ibid., fol. 288v: "Nam in fornacibus, quibus excoquitur aes aut argentum, corpuscula ascendunt non nigra ut resinis, sed luteo colore, aut candicante, aut vario. Haec superioribus fornacis lateribus cohaerentia concrescunt in cadmiam: similiter ex pyrite usto gignitur, ut testatur Dioscorides." Dioscorides, *Materia medica* 5.75.
57 Cesalpino, *DMF*, fol. 288v: "Ex cadmia vero sola aut cum aere sublimata fit pompolyx et spodium. … Quae omnia corpora terrea sunt, caliditatem quandam ex ustione retinentia, sed si abluantur, illam exuunt, et siccant sine morsu."
58 Ibid., fols. 289r–290r.
59 Ibid., fol. 289r: "Sublimatio igitur corporum separat partes exhalabiles, attenuat, et caliditatem auget. Quod si haec fiat per combustionem, immutat naturam corporum in terream substantiam cum quodam ignis vestigio."
60 Ibid., fol. 289r–289v: "Respondet Galenus in libro de Theriaca ad Pisonem in confectione salis theriaci multa ignis commercio reddi meliora, cum latens ipsorum natura in apertum editur. Nonnulla etiam ad quem volumus usum commoda reddi. Quod hinc patet. Nonnulla enim vires novas per ignem acquirunt. … Nonnulla per ignem mitiora sunt et sic usui magis commoda. … Acria omnia per ustionem acrimoniam deponere ac mitescere."; Pseudo-Galen, *De theriaca ad Pisonem* 18 (14:287–90K).

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